A TOXICICITY STUDY

ON

POORA PARPAM

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Introduction

INTRODUCTION

Siddha system of medicine is commonly practiced byTamilians of peninsular South India. Fundamental Principles of Siddha include theories of five elements (*Aimpootham*), and three humors (*Mukkuttram*). Siddha system of medicine not only includes polyherbal formulations, but also metals, chemicals, and/or animal products. The common Siddha preparations are parpam (calcined metals and minerals), Chenduram (red coloured powders), Churanam (powders), Kashayam (decoctions), Lehiyam (confections), Nei (ghee), Tailam (oil), and Mezhugu (wax)[1].Calomel-containing preparations have been used extensively in siddha system of medicine for treatment of chronic ailments like syphilis, high fever, pneumonia, insomnia, nervous disorders,deafness, and paralysis of the tongue. Contrary to Western medicine, which does not promote the use ofmercury due to its toxic effects, Siddha medical practitioners believe that mercury-based formulations have potent therapeutic efficacy, while there is no toxicity due to the unique and repeated purification processes employed during preparation.

However, lack of proper pharmacovigilance and widespread self-medication has resulted in undesirable effects to certain sections of the consumers of these preparations, which have contributed to the negative publicity for these forms of medicine. Variations in the quality of the preparations coupled with the lack of understanding of the differences in the recommended dosages and treatment strategies adopted by traditional medicine practitioners, further fuels concerns in the Western world on the safety and efficacy of traditional medicine. But in spite of these concerns, concerted efforts to understand the biological interactions and transformations of these preparations are yet to gain momentum. Although scattered reports on the toxicity of these preparations are available in literature, their mechanism of action has not been conclusively established [2]. Long-term

pharmacotherapeutic and in-depth toxicity studies are needed to address the apprehensions raised by these herbo-metallic preparations.

This research work aims in evaluating the toxicological effects of Pooraparpam(பூர பற்பம்)- calomel derived drug in albino rats. Calomel was taken internally and used as a laxative and disinfectant, as well as in the treatment of syphilis, until the early 20th century. Until fairly recently it was also used as a horticultural fungicide, most notably as a root dip to help prevent the occurrence of clubroot amongst crops of the Brassicaceae family.[3]

Calomel was used by doctors in America throughout the 18th century, and during the revolution, to make patients regurgitate and release their body from "impurities". Benjamin Rushwas one particular well-known advocate of mercury in medicine and used calomel to treat sufferers of yellow fever during its outbreak in Philadelphia in 1793. Calomel was given to patients as a purgative or cathartic until they began to salivate and was often administered to patients in such great quantities that their hair and teeth fell out.[4] Shortly after yellow fever struck Philadelphia, the disease broke out in Jamaica. A war of words broke out in the newspapers concerning the best treatment for yellow fever; bleeding or calomel. Anecdotal evidence indicates calomel was more effective than bleeding.[5]

Pooraparpam is a calomel-derived drug widely used in therapeutic management of various skin disorders, venereal diseases, metabolic disorders and menstrual disorders. Its use has been described by many sages for treatment of various metabolic disorders including diabetes [6]. In siddha system of medicine calomel is used internally and externallyfor treatment of various genital cancers (லிங்கப் புற்றுமற்றும் யோனிப் புற்று) and syphilitic ulcers (குழிக் கிரந்தி) [6].

Though there are lot of methods described by various sages for preparation of pooraparpam, preparation using piper beetle and crab extract described in Aruvaimaruthuvam is followed in this research work.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE:

CALOMEL:

Mercury(I) chloride is the chemical compound with the formula Hg_2Cl_2. Also known as calomel (a mineral form, rarely found in nature). Mercurous chloride, this dense white or yellowish-white, odourless solid is the principal example of a mercury(I) compound.Various properties of calomel are shown in Table.2.1.

Table 1: Properties of Calomel

Properties	
Molecular formula	Hg_2Cl_2
Molar mass	472.09 g/mol
Appearance	White solid
Density	7.150 g/cm^3
Melting point	525 °C (triple point)
Boiling point	383 °C (sublimes)
Solubility in water	0.2 mg/100 mL
Solubility	insoluble in ethanol, ether
Refractive index	1.973

பூரம்:

பூரத்தின் குணங்கள் பற்றி சித்த மருத்துவத்தில் கூறப்பெற்றுள்ள கருத்துக்களை இங்கு காணலாம்.

பூரத்தின் வெறு பெயர்:

"துர்க்கை களை யெலியிடைச் சனி பூரஞ்....

- *நாமதீப நிகண்டு, பக்கம் 29*

"தீட்டுவிடதாலி நக்கி பூரமதாஞ்.....

- நாமதீப நிகண்டு, பக்கம் 76

பூரத்தினை 64 - பாசாணங்களுள் - சொல்லப்படவில்லை. இருப்பினும் மருத்துவர்களால் பாசாண வகைகள் ஒன்றகவே கருதப்படுகிறது. இது இரசம், உப்பு இவைகளினால் செய்யப்படும் சரக்காகும்.

பூரத்தின் சுவை - உப்பு, கார்ப்பு

வீரியம் - வெப்பம்

பிரிவு - கார்ப்பு

குணம் -*இடைவாத சூலை, யெரிசூலை குன்மந்*

தொடைவாழை வாதமாஞ்சோனி - யிடையாதோ

வொக்குரசு கர்ப்பூர மொன்றே யளவோடுநல்

இக்குவெல்லத் தேழுனாளீ

நல்ல இரசகர்ப்பூரத்தை அளவுடன் கரும்பு வெல்லத்தில் ஏழு நாள் கொடுக்க வெண்டும். இடுப்பைப் பற்றிய சூலை, ஆங்காங்கு எரிச்சலைத் தருகின்ற சூலை, வாத குன்மம், தொடை வாழை,வாத ரத்த நோய் தீரும்.

"கசிவன்ன கரும்பூ ரத்தில் சாதித்த கயஞ்சுவாசம்

பசிகலி தாப சோபம் பவுத்திரம் பிளவை குஷ்டம்

வசிதரு கிராணியோடு வளரதி சார மெகம்

இசிதரு மிசிவு சூலை இவை பல ரோகம் போமே"

"திரண்ட வாதங்குடல் வாதம் தீருஞ் சந்திபதின் மூன்று

மாருண்டே குத்து மரையாப்பு மண்டை சூலை கபால விடி

பரங்கிச் சூலை பற்கிரந்தி பக்கச் சூலை இவை முதல் போம்

இருண்ட மேனி பொன்னிறமாம் இதுவே கற்பம் இயம்பீரே"

சுரம், மஞ்சட்காமாலை, பித்த தோடம், சீத பேதி, நீர்க்கோவை, விரண சந்தி, ஆறாத விரணங்கள், மேக வியாதிகள், கல்லீரல் வீக்கம், குழந்தைகளுக்குண்டாம் பேதி, கிருமி நோய், கீல் வாதம், சொறி சிரங்கு, மலபந்தம், தலைவலி தீரும்.

“வீதமென்ற வீரவைப்புகை முறையாய்ச் சொன்னேன்

விருதான பூரணவ்வைப்பை விளம்பக்கேளு

நேரமில்லை முன் செய்த சூதமாவில்

நிறுத்தெடுத்து நாலு பங்கு குப்பிக் கேற்றி

பாரமில்லா வாலுகையிற் காலம் பொலே

பதமாக எரிக்கயெலே யுருகும்பாரு

வோரமில்லை யுருகுபதந்தன்னைக்கான

உறுதியுடனிருசாம மெரித்து மேலே

மேலாகச் சலாக்கையீட்டு கிண்டிப்பாரு

மேன்மையுடன் னுருகிக் குழம்பு போலாம்

காலான சீன்மரை பலத்தைத்தானுங்

காணக்காப் பொடிதனிலே போட்டுக் கிண்டி

நாலான சாம மட்டு மெரித்து நீயும்

தன்மையுடன் சிலாகையிட்டு பார்த்தாயானால்

கேலான அடியில் மருந்தில்லாவிட்டால்

குருவான பதமென்று குணமாயாற்றே

ஆற்றியெகுப்பிதனையுடைத்துப்பாரு

அப்பனேவெள்ளையாயிருக்குஞ்சொன்னேன்

போற்றியேபூரமதைப்பதனம்பண்ணு

புண்ணியனே யின்னமொருவிந்தைக்கேளு

சாற்றுகிறேன்ஆரலத்திப்பூரவைப்பை

தன்மையுடன்னுரைக்கத்தயவாய்க்கேளு

மேற்றோவைப்போக்கினதோர்முத்தக்காசு

விளங்கியலவங்கமிடைவராகன்பத்தே

பத்தானசீனம஼திரண்டுபத்துப்

பாங்கானவெடியுப்புநூறுங்கட்டி

பாங்கானகலிவத்திற்பொடித்துக்கொண்டு

சிவந்தகருவாய்பட்டைத்தைலம்வாங்கி

முத்தானமிச்சாமமரைத்துமைந்தா

முறையுடனேபிட்டுபோலுதிர்த்துநான்கு

வற்றாதகங்காலக்குப்பிதன்னில்

மார்க்கமுடனரைவாசியடைத்துக்கேளே

கேளப்பாமரக்கல்லாவரைத்துநீயும்

கிருபையுடனெழுசீலைமண்ணுஞ்செய்து

நாளப்பாநன்றாகக் காயவைத்து

நாதாந்தவாலைபதநாடிநின்று

வாளப்பா வால்லுகையிரற் பாண்டம் வைத்து

விதமாக ஆறுவிதமணல் தாவிட்டு

வாளப்பா குப்பிதனை மேலேயிட்டு

வன்மையுடன் பானைரம்பமணலால்மூடே

மூடியேயடுப்போற்றிக்கமலம்போலே

மூர்க்கமுடனேருதாழியெரித்துப்பாரு

நாடியேமணறிகுடுநிரம்பவானால்

நன்மையுடன்பாண்டமதையிறக்கிவைத்துக்

கூடியேகுளிரநன்றாயாரவிட்டுக்

குருவானகுப்பிதனையுடைத்துப்பாரு

தேடியேயலைந்தாலுமித்தப்பூரம்

தேசத்தில்விபரீதமென்பார்கானே

- அகஸ்தியர்பரிபூரணம்

இரசகற்பூரம்வைப்பு

மயக்கமறுமிரசகற்பூரஞ்சொல்வோம்வந்ததொருவியாதிபோம்
வரிசைகேளு

மயக்கமறஉப்புக்குச்செங்கல்தூளும்வரிசைபெறவுழக்கொடுத்து
வைத்திடாயே

வைத்ததோரிருவையுந்துளாயாட்டிமைந்தனேசட்டிக்குள்பரத்திநீயும்

வைத்திடுவாயதில்குகையைச்குதம்ப்பாவாரடாகழஞ்சுபத்துமாற்றமின்றி

வைதாங்கேகுகைவாயில்பொடியுமிட்டுமறுசட்டிக்கொண்டிட்டு
வானைமூடி

வைத்துநீஏழுசீலைமண்ணுஞ்ச்செய்துமாயிபதம்பூசித்து
அடுப்பிலேற்றே

அடுப்பேற்றிக்கமலவன்னிதினந்தொனொன்றுஅதன்பிறகு
காடக்கிணியுந்தான்
மூன்றுகடுப்பமுடநாலுநாள்சென்றபின்புகன்றினுடசாணியிந்தக்
காட்டுமண்ணு

தடுப்பாலேகட்டிநீதண்ணிருற்றிநன்றாகச்சுவரியபின்சீலைகொண்டு

வடுப்பாகதேவாங்குபின்னுங்கேளுமருபடியும்நீர்விட்டுயெரித்திடாயே

எறித்தாறியெடுத்துப்பார்சட்டிமெலேஏறிநிற்க்கும்கற்பூரமெடுத்துவைத்து

அரிந்திடுமேநாய்குலைமண்டைகுலையப்பனேநாசிப்புண்
தொண்டைப்புண்ணும்

பரிந்திடுமேநாசிநீர்கண்ணில்நீரும்பாங்கானதேனிலேகொள்ளத்திரு

மெரித்திட வேயிடையேதுபணத்திற்பாதியூட்டாகுலைமுதல்
புண்ணும்போமே

புன்போகுங்குன்மத்துக்கனுபானங்கேள்பொடி செய்துதிரிகடுகுபணந்தான்

மூன்று

புன்பாகக்கற்பூரமரைப்பானந்தான்தேனில்பாச்சாவேகுன்மமெல்லாம்
பறந்துபோகும்

கன்பாகச்சூலைக்குவெள்ளைவாய்பிசினுங்கடுசுக்குகியாமம்
வெள்ளுள்ளியாதலால்

உண்பதற்குக்கொடுத்திட வேநீவிர்த்தியாகுமோடுகிறகிராணிக்கு
வுண்மைக்கேளே

--அகஸ்தியமுனிவரருளிச்செய்தவைத்தியகாவியம் 1500

பூரம்(இரசக்கற்பூரம்)

பூரவைப்பு – செய்முறை

1. பாண்டதில் 16 வராகனெடை (627 கிராம்) கந்தகம் வைத்துருக்கி, 80 வரகனெடை(336 கிராம்) இரசம்சேர்த்துத்துளாவிக்கொண்டிருந்தால், கறுத்துவிடும்பிறகுவேறொருபாண்டத்தில்பாதிக்குச்செங்கல்பொடியைப்போட்டு, அதன்மேல்அரைப்படி(650 மி.லிட்டர்) கறியுப்பைவைத்து, உப்பின்மேல்மேற்படிஇரசகந்தியைவைத்து, சீலைமண்செய்து, 12 மணிநேரம்காடக்கினியாய்எரித்துஎடுத்துகுளிர்ந்தபிறகுமேல்பாண்டத்தைச்சாக்கிரதையாய்நீக்கிப்பார்த்தால்பூரம்கட்டியாய்ப்படிந்திருக்கும்.

பூரம்சுத்திமுறைகள்:

1. கம்மாறுவெற்றிலை, மிளகுவகைக்குகால்பலம் (8.75 கிராம்) நிறுத்தெடுத்துச்சிறிதுநீர்விட்டுஅரைத்து, கல்கத்தைஒருபடி (1.3 லிட்டர்)நீரில்கலந்துஒருபலம் (35 கிராம்) பூரத்தைச்சீலையில்முடித்துதுலாயந்திரமாய்நீரில்அமிழும்படிசெய்து,. நீர்முக்காற்பங்குசுண்டியபிறகு, பூரத்தைஎடுத்துநீர்விட்டுக்கழுவிவெயிலில்உலர்த்திஎடுக்கவெண்டும்.
2. ஒருபலம் (35 கிராம்) பூரத்திற்குமுலைப்பாலினால்முன்றுமணிநேரம்சுருக்குக்கொடுத்துபிற குவெள்ளைப்பூண்டுதைலத்தினால்ஒன்பதுமணிநேரம்சுருக்கிட்டுஎடுத் துக்கொள்ளவும்.
3. இலேகியங்களில்சேர்க்கவெண்டியபூரத்தை முசுமுசுக்கைச் சாற்றினால்சுருக்கிட்டுகழுவவும்.

- குணபாடம்தாதுஜீவவகுப்பு

4. இரசக்கற்பூரம் 1 பலம்இதனைமெல்லியதுணியில்கிழிகட்டிக்கொள்ளவெண்டும். ஒருமண்பாண்டத்தில்இரண்டுபடிபசுவின்பாலைவிட்டுஅதில் 5 பலம்கஞ்சாவைத்தூள்செய்துஅல்லதுதண்ணீர்விட்டரைத்துகரைத்துமு ன்முடிப்பை பானைக்குள்தொங்கவிடவேண்டும் . முடிப்பானதுபானையின்அடியில்படாமல்பால்சுண்டி ¼ படியாகஇருக்கும்போதுஇறக்கிஆறியபின்இரசக்கற்பூரத்தைஎடுத்துக் கொள்ளவெண்டும். இவ்விதமேமடக்கிமடக்கிமூன்றுதடவைகள்செய்யின்இரசக்கற்பூரமான துதூய்மையாகிவிடும். வாய்பிடிக்கும்குணமுள்ளசர்க்காகையால்இதனைமேற்கண்டபடிதூய் மைசெய்வதால்அந்ததீயகுணம்நின்றுபோகும்.

- அனுபோகவைத்தியநவநீதம் - 4ம்பாகம்பக்கம் - 91

பூரம்கொண்டுசெய்யப்படும்மருந்துகள்

பூரபற்பம்:

சுத்திசெய்தபூரத்தைகல்வத்திலிட்டுஏழுநாள்நன்றாகஅரைத்துப்பிறகுசே கரித்துக்கொள்ளவும். இதுவேபூரபற்பமென்றுகையாளாப்படுகின்றது.

அளவு

அரைஉளுந்தெடை (32 மி.கிராம்) யிலிருந்துமூன்றுஉளுந்தெடை (195மி.கிராம்) வரைஉபயோகிக்கலாம். இரண்டுஉளுந்தெடை (130 மி.கிராம்)க்குமேற்படக்கொடுத்தால்பேதியாகும்.

துணைமருந்தும், தீரும்நோய்களும்:

கரும்புவெல்லத்தில்ஏழுநாள்அருந்த,
பொதுகுணத்தின்கீழ்க்கூரப்பட்டநோய்கள்நீங்கும்.

பூரம்சேரும்பிறமருந்துகள்

வெள்ளெழுத்துத்தைலம்

ஆடுதின்னாப்பாளைமூலம்

கவிழ்தும்பை-இரண்டையும்நிழலிலுலர்திக்கஷாயமாக்கி2படி
எடுத்துக்கொள்ளவும்.

நல்லெண்ணெய் - 1படி

மிளகு, மஞ்சள், சம்பிராணி, பூரம், கோஷ்டம்வகைக்கு ¼ பலம்சேர்த்துகாய்ச்சிமெழுகுபதத்தில்வடித்திடவும்.

தீரும்நோய்:

வாரமிருமுறைதலைக்குதேய்த்துக்குளித்துவரகண்ணில்வந்தமாசிதீரும். வெள்ளெழுத்துக், கண்மங்கல்விலகியோடும். பித்தமொடுகுன்மங்கள்மகோதரங்கள்தீரும்.

பூரக்கட்டு

ஒருபலம் (35 கிராம்) பூரக்கட்டியை, முலைப்பாலிட்டுப்பத்துநாள்ஊறவைத்துஉலர்த்திஎடுத்துக்கொள்ளவும்.

வெள்ளைப்பூண்டுத்தைலத்தினால்மேற்படி கட்டிக்கு மூன்று சாமம் (9மணி) சுருக்குக் கொடுத்துச் சுரண்டி ஒர் ஓட்டில் வெடியுப்பு ஐந்து பலம் (175 கிராம்) பரப்பி, அதன்மேல் ஊற்றி வாசலில் அடுப்பிட்டுக் கால் நாழிகை கமலம் போல் எரிக்க உப்பு உருகி நெருப்பு பற்றும். அண்டத்தின் மகிமையால் குழம்பு போல உருகிக் கெட்டியாகும். ஓட்டினை இறக்கிக் குளிர்ந்த பின்பு உடைந்துப் பூரக்கட்டியை எடுத்துக் கொள்ளவும்.

தீரும் நோய்:

தக்க அனுபானத்தில் கட்டினை உரைத்துக் கொடுக்க சன்னிசுரம், நாவறட்சி, மலவாதசந்தி நீங்கும்.

பூரக்கட்டு

சாம்பிராணி, கருப்பூரம் இரண்டையும் சமனாய் சேர்த்தரைத்து, ஒரு பலம் (35 கிராம்) பூரக்கட்டியின் மேல் கவசமிட்டு, உலர்த்திக் கொடுத்தி எரித்த பிறகு, கவசத்தை நீக்கி விட்டுச் சரக்கை எடுத்துக் கொள்ளவும்.

பூரக்கட்டு (வேறு)

வெள்வங்கம், சவ்வீரம், பொட்டிலுப்பு சமவெடை கட்டி அரைக்கச் செய்நீரகும். இதைக் கொண்டு அப்பிரகத் தகட்டிலிட்ட பூரத்திற்குச் சுருக்கு கொடுத்து, சரக்கை எருக்கம் வேருக்குள் வைத்துச் சீலை மண் செய்து முழப்புடத்தில் வைத்து எரித்து எடுத்துக் கொள்ளவும்.

இரசக் கற்பூரக் குளிகை:

முலைப்பாலில் மூன்று நாள் ஊரின பூரம் ஐந்து வராகனெடை(21 கிராம்) முலை நீக்கிய வெள்ளைப்பூண்டு 20 வராகனெடை (84 கிராம்) மிளகு 30 வராகனெடை, வெற்றிலை 40 வராகனெடை சேர்த்து வெற்றிலைச் சாறு விட்டு ஐந்து சாமம் (15மணி) அரைத்து, சுண்டைக்காய் போல் உருட்டி நிழலில் உலர்த்தி கொள்ளவும்.

அளவு

ஒரு மாத்திரை இருவேளையாய் எழு நாள் அருந்தவும்.

பத்தியம்

உப்பு, புளி நீக்கவும்.

ஒரு வேளை பசும்பால் சேர்த்துக் கொள்ளவும். எழு நாள் சென்ற பிறகு வறுத்த உப்பு, துவரை கூட்டி பதினைந்தாம் நாள் ஓமம் தேய்த்துத் தலை முழுகிப் புளி கூட்டவும். பிறகு எண்ணெயிட்டு முழுகவும்.

தீரும் நோய்:

வளிக் கிரந்தி, இலிங்கப்புற்று, சொறி, கிரந்தி, யோனிப்புற்று குழிப்பட்ட விரணம், குழிக்கிரந்தி முதலியன போம்.

கண்ணுசாமியம் என்னும் வைத்திய சேகரம் என்ற நூலில்

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முப்பு செய்ய பூரம் பயன்படுவது பற்றி கூறப்பட்டுள்ளது.

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யாக்கோபு காண்டம் என்ற நூலில்

"தொடுத்திட்ட வீரமொடு பூரந்தானும் ..... 70ம் பாடம்

சயகாசத்துக்குச் செந்தூரம்

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டிபிள்ளை சாம்பசிவம் .வி. 5ம்-பாகம் என்ற நூலின்- பக்கம் 3821

"சாரத்தை விட்டால் செயனீரில்லை

காரத்தை விட்டால் உருக்கினமில்லை

தாரத்தை விட்டால் களங்கில்லை

வீரத்தை விட்டால் மனிகளில்லை

பூரத்தை விட்டால் குருவுகளில்லை"

மேற்கண்ட வரிகள் மூலம் பூரம் குரு செய்வதர்க்கு பயன்படும் என்பது புலனாகிறது.

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ஆத்மரட்சாமிர்த வைத்திய சாரசங்கிரகம் என்ற நூலில்

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PIPER BETEL:

Since antiquity, Piper betel Linn (betel vine; family Piperaceae) has been an important medicinal agent in the various traditional and folk systems of medicine in SoutheastAsian countries. The leaves are the most valued plant part and in the past were routinely used as a chewing agent to prevent halitosis. The leaves are also supposed to harden the gum, conserve the teeth and to prevent indigestion, bronchitis, constipation, congestion, coughs and asthma. Innumerable scientificstudies have

validatedtheethno medicinalclaims. Betel leavesarean integral component of the betel quid that consists of areca nut (Areca catechu Linn.), tobacco (Nicotianatabacum L) and slaked lime; a highly abused agent with carcinogenic properties. Regular chewing of betel quid is associated mainly with oral cancer and detail studies with individual constituents of the quid have shown that both tobacco and areca nut are carcinogenic, while slaked lime is shown to promote the process of carcinogenesis.

Table 2: Chemical Constituents of Piper betel[9]

S.No	Compound	Activity	Mode of action
1	Hydroxy -chavicol	Hyperuremia (antidiabetic), immunomodulatory, inhibits platelet aggregation	A potent COX-1/COX-2-inhibitors, ROS scavenger and inhibits platelet calcium singnalling, TXB production and aggregation
2	Allylpyro-catechol	Gastric ulcerhealing action, anti-inflammatory effect	Inflammatory response of macrophages via inhibition of iNOS, COX-2 and IL-12 p40 through down regulation of the NFkappaB pathway
3	Chavi-betol	Radioprotective activity	Protects photsensitization-mediated lipid peroxidation of rat liver
4	Piperbetol	Platelet Hyperactivity	Selectively inhibits platelet aggregation factor

However unlike other constituents of the betel quid, the betel leaves devoid carcinogenic effects and on the contrary possesses cancer preventive effects including against the carcinogens present in tobacco. Subsequent studies have conclusively

shown that the betel leaf and some of its phytochemicals also prevented chemical induced cancers in experimental animals [8].

The main chemical constituents of piper betel leaves include Hydroxychavicol (HC)/ Hydroxychavicol acetate(HCA), Allylpyrocatechol (APC), Chavibetol (CHV), Piperbetol, arecoline, carvacrol, caryophyllene, piperitol, piperbetol, eugenol, isoeugenol, allylpyrocatechol, chavicol, safrole, anethole. Chavibetol, cadinene.Hydroxychavicol.β-sitosterol,β-sitosterylpalmitate, dotriacontanoic acid, tritriacontane, stearic acid, cepharadione, piperine, piperlonguminine. Chavibetol acetate, allylpyrocatecholmonoacetate.allyldiacetoxy benzene.estragole, methyl eugenol and hydroxycatechol.methylpiperbetol, piperol A and piperol B. cavacrol, eugenol acetate, and allylpyrocatecholdiacetate[9].

வெற்றிலைகுணம் –

இனிசித்தமருத்துவத்தில்வெற்றிலைபற்றிகூறப்பட்டுள்ளகருத்துகளை காண்போம்.

> “ஐயம்அறுங்காண்அதன்சாரங்கொண்டக்காற்
> பையச்சயித்தியம்போம்பைந்தோடியே! – மெய்யின்
> கடியின்குணம்போகுங்காரவெற்றிலைக்குப்
> படியுமுத்தோடமிதைப்பார்.”
>
> - அகஸ்தியர்குணவாடகம்

மேற்கண்ட பாடல் மூலம் வெற்றிலையின் இரசத்தைப் பருகில் , ,ஐயம், முப்பிணி, காணாக்கடி, சயித்தியம், முதலியன குணமாகும் என்று அறியப்படுகின்றது

சுவை: கார்ப்பு, விறுவிறுப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

செய்கை:வெப்பமுண்டாக்கி ,பெருக்கி காமம் ,துவர்ப்பி ,அகட்டுவாய்வகற்றி , ,வெப்பகற்றி ,அழுகலகற்றிபசித்தீத்தூண்டிஉமிழ்நீர்ப்பெருக்கி ,பாற்பெருக்கி ,

PIPER NIGRUM:

Black pepper (*Piper nigrum*) is a flowering vine in the family Piperaceae, cultivated for its fruit, which is usually dried and used as a spice. The fruit, known as a peppercorn when dried, is approximately 5 millimetres (0.20 in) in diameter, dark red when fully mature, and, like alldrupes, contains a single seed. Peppercorns, and the powdered pepper derived from grinding them, may be described simply as pepper or more precisely as black pepper (cooked and dried unripe fruit), green pepper (dried unripe fruit) and white pepper (dried ripe seeds).

Black pepper is native to south India, and is extensively cultivated there and elsewhere in tropical regions. Currently Vietnam is the world's largest producer and exporter of pepper, producing 34% of the world's *Piper nigrum* crop as of 2008.

Dried ground pepper has been used since antiquity for both its flavour and as a medicine. Black pepper is the world's most traded spice. It is one of the most common spices added to European cuisine and its descendants. The spiciness of black pepper is due to the chemical piperine. It is ubiquitous in the industrialized world, often paired with table salt.

Piper nigrum, commonly is used as a stimulant and carminative and prescribed for cholera, dyspepsia, flatulence, diarrhoea and various gastric ailments. Several alkaloids and non-alkaloidal constituents have been reported from this plant. More than 40 compounds has been isolated from piper nigrum.

மிளகின்பெருமை:

“தீயாகியெங்கும்திரியுமதையாவத்து

மோயாமலெப்படியும்முண்டாக்காற் – பாயாது

போந்திமிர்வாதங்கிரந்திபுண்ணீரும்மண்ணவர்க்கும்

காந்திமெய்வாதச்சலுப்பைக்காய்.”

இதன்மூலம்மிளகுவளி, தீ, கபகுற்றங்கள்அனைத்தையும்நீக்கும்என்றும்திமிர்வாதம், கழலை, வளி, சளிஇவைகலையும்போக்கும்என்றும்அறியப்படுகிறது.

சுவை: கைப்பு, கார்ப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

செய்கை: காறலுண்டாக்கி, அகட்டுவாய்வகற்றி, முறைவெப்பகற்றி, தடிப்புண்டாக்கி, வெப்பமுண்டாக்கி, வீக்கங்கரைச்சி, வாதமடக்கி, நச்சரி.

வயல் நண்டு:

வயல் நண்டின் மருத்துவ குணம் பற்றி நவீன அறிவியலில் தெளிவான கருத்துகள் எதுவும் கூறப்படவில்லை. எனவே அதன் சிறப்பு பற்றி சித்த மருத்துவத்தில் கூறப்பட்டுள்ளவை மட்டும் கீழே கொடுக்கப்பட்டுள்ளன.

வேறு பெயர்:

களவன், குளிரம், நள்ளி, கவைத்தாள், கர்க்கடகம், அலவன்

சிறந்தது:

பால் நண்டு

செய்கை:

பித்தமகற்றி, சிறுநீர்ப் பெருக்கி, மலமிளக்கி, குருதிப்பெருக்கி, இதய வெப்பமுண்டாக்கி

குணம்:

“வயலிலுறு நண்டருந்த வாதக் குடைச்ச

லயலி லிருக்கா தணங்கே – துயிலவொட்டா

வன்சயித்தி யங்கரப்பான் மங்குடலி ரைச்சலும்போ

முன்பயித்தி யங்கதிக்கு முன்”

இந்த பாடல் மூலம் வயல் நண்டு வாத குடைச்சல், தூங்கவிடாதபடி செய்யும் அதி சீதளம், கரப்பான், நிலைபெற்ற குடலிரைச்சல் முதலியன போகும் என்றும், பித்தம் பெருகும் என்றும் அறியப்படுகின்றது.

CURCUMA LONGA(பசு மஞ்சள்)

Curcuma longa, a perennial herb and member of the Zingiberaceae (ginger) family, grows to a height of three to five feet and is cultivated extensively in Asia, India, China, and other countries with a tropical climate. It has oblong, pointed leaves and funnel-shaped yellow flowers. The rhizome, the portion of the plant used medicinally, is usually boiled, cleaned, and dried, yielding a yellow powder. Dried Curcuma longa is the source of the spice turmeric, the ingredient that gives curry powder its characteristic yellow colour. Turmeric is used extensively in foods for itsflavour and colour, as well as having a long tradition of use in the Chinese and siddha systems of medicine, particularly as an anti-inflammatory and for the treatment of flatulence, jaundice, menstrual difficulties, hematuria, hemorrhage, and colic. Turmeric can also be applied topically in poultices to relieve pain and inflammation. Current research has focused on turmeric’s antioxidant, hepatoprotective, anti-inflammatory, anticarcinogenic, and antimicrobial properties, in addition to its use in cardiovascular disease and gastrointestinal disorders[10].

ACTIVE CONSTITUENTS:

The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and

zingiberone. Other constituents include sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprises 0.3-5.4 percent of raw turmeric.

Pharmacokinetics

Pharmacokinetic studies in animals have demonstrated that 40-85 percent of an oral dose of curcumin passes through the gastrointestinal tract unchanged, with most of the absorbed flavonoid being metabolized in the intestinal mucosa and liver.

Due to its low rate of absorption, curcumin is often formulated with bromelain for increased absorption and enhanced anti-inflammatory effect.

Mechanisms of Action

Antioxidant Effects

Water- and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to vitamins C and E. A study of ischemia in the feline heart demonstrated that curcuminpretreatment decreased ischemia-induced changes in the heart. An in vitro study measuring the effect of curcumin on endothelial heme oxygenase-1, an induciblestress protein, was conducted utilizing bovine aortic endothelial cells. Incubation (18 hours) with curcumin resulted in enhanced cellular resistance to oxidative damage.

Hepatoprotective Effects

Turmeric has been found to have a hepatoprotective characteristic similar to silymarin. Animal studies have demonstrated turmeric's hepatoprotective effects from a variety of hepatotoxic insults, including carbon tetrachloride (CCl),galactosamine, acetaminophen (paracetamol), and Aspergillusaflatoxin. Turmeric's hepatoprotective effect is mainly a result of its antioxidant properties, as well as its ability to decrease the formation of proinflammatory cytokines. In rats with CCl-induced acute and subacute liver injury, curcumin administration significantly decreased liver injury in test animals compared to controls. Turmeric extract inhibited fungal aflatoxin production by 90 percent when given to ducklingsinfected with Aspergillusparasiticus. Turmeric and curcumin also reversed biliary hyperplasia, fatty changes, and necrosis induced by aflatoxin production. Sodium curcuminate, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, and bilirubin, as well as increasing bile solubility, therefore possibly preventing and treating cholelithiasis.

Anti-inflammatory Effects

The volatile oils and curcumin of Curcuma longa exhibit potent anti-inflammatory effects. Oral administration of curcumin in instances of acute inflammation was found to be as effective as cortisone or phenylbutazone, and one-half as effective in cases of chronic inflammation. In rats with Freund's adjuvant-induced arthritis, oral administration of Curcuma longa significantly reduced inflammatory swelling compared to controls. In monkeys, curcumin inhibited neutrophil aggregation associated with inflammation. C. longa's antiinflammatory properties may be attributed to its ability to inhibit both biosynthesis of inflammatory prostaglandins from arachidonic acid, and

neutrophil function during inflammatory states. Curcumin may also be applied topically to counteract inflammation and irritation associated with inflammatory skin conditions and allergies, although care must be used to prevent staining of clothing from the yellow pigment.

Anticarcinogenic Effects

Animal studies involving rats and mice, as well as in vitro studies utilizing human cell lines, have demonstrated curcumin's ability to inhibit carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth. In two studies of colon and prostate cancer, curcumin inhibited cell proliferation and tumor growth. Turmeric and curcumin are also capable of suppressing the activity of several common mutagens and carcinogens in a variety of cell types in both in vitro and in vivo studies. The anticarcinogenic effects of turmeric and curcumin are due to direct antioxidant and free-radical scavenging effects, as well as their ability to indirectly increase glutathione levels, thereby aiding in hepatic detoxification of mutagens and carcinogens, and inhibiting nitrosamine formation.

Antimicrobial Effects

Turmeric extract and the essential oil of Curcuma longa inhibit the growth of a variety of bacteria, parasites, and pathogenic fungi. A study of chicks infected with the caecal parasite Eimera maxima demonstrated that diets supplemented with 1-percent turmeric resulted in a reduction in small intestinal lesion scores and improved weight gain. Another animal study, in which guinea

pigs were infected with either dermatophytes, pathogenic molds, or yeast, found that topically applied turmeric oil inhibiteddermatophytes and pathogenic fungi, but neither curcumin nor turmeric oil affected the yeast isolates. Improvements in lesions were observed in the dermatophyte- and fungi-infected guinea pigs, and at seven days post-turmeric application the lesions disappeared. Curcumin has also been found to have moderate activity against Plasmodium falciparum and Leishmania major organisms.

Cardiovascular Effects

Turmeric's protective effects on the cardiovascular system include lowering cholesterol and triglyceride levels, decreasing susceptibility of low density lipoprotein (LDL) to lipid peroxidation, and inhibiting platelet aggregation. These effects have been noted even with low doses of turmeric. A study of 18 atherosclerotic rabbits given low-dose (1.6-3.2 mg/kg body weight daily) turmeric extract demonstrated decreased susceptibility of LDL to lipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels. The higher dose did not decrease lipid peroxidation of LDL, but cholesterol and triglyceride level decreases were noted, although to a lesser degree than with the lower dose. Turmeric extract's effect on cholesterol levels may be due to decreased cholesterol uptake in the intestines and increased conversion of cholesterol to bile acids in the liver. Inhibition of platelet aggregation by C.longa constituents is thought to be via potentiation of prostacyclin synthesis and inhibition of thromboxane synthesis.

Gastrointestinal Effects

Constituents of Curcuma longa exert several protective effects on the gastrointestinal tract. Sodium curcuminate inhibited intestinal spasm and p-tolymethylcarbinol, a turmeric component, increased gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric has also been shown to inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine, significantly increasing gastric wall mucus in rats subjected to these gastrointestinal insults[10].

பசு மஞ்சள்:

வேறு பெயர்: அரிசனம், கான்சனி, நிசி, பீதம்

இதன் கிழங்கிற்கு மஞ்சள் என்று பெயர்.இதற்கு ஒருவித மணமுண்டு. இது இரு வகைபடும்

1.கப்புமஞ்சள்

2.கறிமஞ்சள்

சுவை: கார்ப்பு,கைப்பு

தன்மை: வெப்பம்

பிரிவு: கார்ப்பு

செய்கை: மணமூட்டி, அகட்டுவாய்வகற்றி, வெப்பமுண்டாக்கி, ஈரல்தெற்றி

குணம்:

“தலைவலிநீ ரேற்றஞ் சளையாத மேகம்
உலைவுதரு பீனசத்தி னூடே-வலிசுரப்பு
விஞ்சு கடிவிடம் வீறுவிர ணங்களும்போம்
மஞ்சள் கிழங்குக்கு மால்.”

1. மஞ்சளை பொடித்து புண்கள் மீது தூவ, அவைகல் ஆறூம்.
2. சாதத்துடன் மஞ்சளைச் சேர்த்து அரைத்து கட்டிகளின் மீது வைத்து கட்ட அவை பழுத்து உடையும்.

மஞ்சளை சுட்டு முகர நீரேற்றம் நீங்கும்.

MERCURY - TOXICOLOGY:

Mercury is a heavy metal of known toxicity, noted for inducing public health disasters. The clinical impact of smaller mercury exposures remains controversial. It exists in several forms: inorganic mercury, which includes metallic mercury and mercury vapour (Hg0) and mercurous (Hg2++) or mercuric (Hg++) salts; and organic mercury, which includes compounds in which mercury is bonded to a structure containing carbon atoms (methyl, ethyl, phenyl, or similar groups). The biological behaviour,pharmacokinetics, and clinical significance of the various forms of mercury vary with chemical structure. There is some inter conversion in vivo between the various forms of mercury. Inhaled elemental mercury vapour, for example, is easily absorbed through mucus membranes and the lung and rapidly oxidized to other forms (but not so quickly as to prevent considerable deposition of elemental mercury in the brain). Methyl mercury is easily absorbed through the gut and deposits in many tissues, but does not cross the blood-brain barrier as efficiently as elemental mercury; however, on entering the brain it is progressively demethylated to elemental mercury. Mercury salts, in contrast, tend to be insoluble, relatively stable, and poorly absorbed. Human toxicity varies with the form of mercury, the dose and the rate of exposure. The target organ for inhaled mercury vapour is primarily the brain. Mercurous and mercuric salts chiefly damage the gut lining and kidney, while methyl mercury is widely distributed throughout the body. Toxicity varies with dosage: large acute

exposures to elemental mercury vapour induce severe pneumonitis, which in extreme cases can be fatal. Low-grade chronic exposure to elemental or other forms of mercury induces subtler symptoms and clinical findings, as discussed hereinafter. There is considerable controversy about the clinical significance of exposure to the various forms of mercury and some disagreement regarding techniques for clinical assessment of mercury burden[12].

Mercury exists in nature primarily as elemental mercuryor as a sulfide and is found in the earth's crust at approximately0.5 parts per million. Atmospheric exposuresoccur from outgassing from rock or through volcanic activity.Human sources of atmospheric mercury include coalburning and mining (mercury and gold in particular).Atmospheric elemental mercury settles in water, where it isconverted by microorganisms into organic (methyl or ethyl)mercury, which is ingested by smaller creatures which areeventually consumed by larger fish. Fish at the top of thefood chain (e.g., tuna, swordfish, or shark) may concentrateconsiderable mercury in their tissues.Human mercury exposures occur chiefly throughinhalation of elemental mercury vapour via occupational ordental amalgam exposure or through ingestion of mercurybonded to organic moieties (methyl, dimethyl, or ethylmercury), primarily from seafood. Most human metallicmercury exposure comes from mercury vapour outgassingfrom amalgam fillings, at a rate of 2 to 28 microgramsper facet surface per day, of which about 80% is absorbed,according to the World Health Organization. A less common source of mercury vapouris spilled mercury, and there is a report in the literatureof Idiopathic Thrombocytopenic Purpura caused byvacuuming spilled mercury (thereby producing a majoracute exposure to mercury vapour).Methyl and dimethyl mercury (organic mercury) usuallyoriginate from biological sources, chiefly fresh or salt waterfish. Over three thousand lakes in the United States havebeen closed

to fishing due to mercury contamination and many species of ocean fish are also tainted with considerableconcentrations of mercury [13].

PHARMACOKINETICS OFMERCURY EXPOSURE

Inorganic Mercury

Elemental or Metallic (Hg0) Mercury: Approximately80% of metallic mercury vapour outgassed from amalgamsis absorbed through inhalation, compared with a bout 7 to 10% absorption of ingested metallic mercury, and about 1% absorption of metallic mercury throughskin contact. On entry to the body, mercury vapour hasgreat affinity for sulfhydryl groups and bonds to sulfur-containingamino acids throughout the body. Mercury vapouris transported to the brain, either dissolved in serumor adherent to red cell membranes. Metallic mercury passeseasily through the blood brain barrier and through theplacenta, where it lodges in the fetal brain.Metallic mercuryis, however, rapidly oxidized to mercuric mercury onentry to the blood stream, although not so quickly as toprevent considerable uptake by the central nervous system while still in the metallic form.In addition to the brain, metallic mercuryis also deposited in the thyroid, breast,myocardium, muscles, adrenals, liver, kidneys, skin ,sweat glands , pancreas , enterocytes, lungs, salivary glands, testes, and prostate andmay be associated with dysfunction of those organs.Mercuryalso has affinity for binding sites on the surface of T cells andfor sulfhydryl groups influencing T cell function.Mercury deposits readily in placenta and fetal tissues and isfound in breast milk.Metallic mercury is largely excreted as mercuric mercury. The excretory half-lives ofmetallic and mercuric mercuryvary widely, depending on the organ of deposition and redoxstate, with values ranging from a few days to several months,

with some pools (e.g., CNS) having a half-life exceedingseveral years. Hair mercury does not correlate withbrain content of metallic mercury. These complexitiesmake accurate assessment of body burden challenging[13].

Mercurous (Hg2++) Mercury:

Mercurous mercury salt in the form of Hg2Cl2 (calomel) is poorly soluble in water and poorly absorbed by the intestine, although some portion is thought to undergo oxidation to more readily absorbable forms. It is doubtful thatmercurous mercury survives in the body, other than as a transitional form between metallic and mercuric mercury. Some absorption evidently occurs, however, as calomel is occasionally associated with pink disease, or acrodynia.

Mercuric (Hg++) Mercury:

Historically, mercuric chloride (HgCl2) was used as a preservative and for development of photographic film and was ingested accidentally or as a suicide measure. It is a component of some skin-lightening creams. Only about 2% of ingested mercuric chloride is absorbed initially, although it is believed that its corrosive effect on the intestine may increase permeability and, hence, absorption, with prolonged exposure. Available data on skin penetration of mercuricmercury are insufficient to make quantitative comparison with ingestion or with metallic mercury. Like metallic mercury, mercuric mercury in the bloodstream adheres to sulfhydryl groups on erythrocytes, metallothionein, or glutathione or is suspended in plasma. Mercuric mercury does not cross the blood-brain barrier efficiently, but it does accumulate in quantity in the placenta, fetal tissues, and amniotic fluid. Evidence exists showing transport of mercuric mercury via one or more amino acid transporters,particularly that for cysteine, which may account for accumulation in the brain. Much of the body burden of mercuric mercury resides in the proximal

convoluted renal tubule bonded to metallothionein. Significant deposition also occursperiportally in the liver and lesser amounts in epithelial tissues, choroidal plexus, and testes. Excretion of mercuric mercury is largely through urine and stool, although significant amounts are shed through sweat, tears, breast milk, and saliva. Half -lives appearto be multiphasic, as with metallic mercury, with humanstudies suggesting an effective half-life of 42 days for 80%of an oral tracer dose; the other 20% did not appear tohave a measureable rate of excretion. This may reflectdemethylation to metallic mercury in the brain and otherorgans or mechanisms yet to be determined.

Organic Mercury Compounds:

Most available data onorganic mercury compounds refer to methyl mercury, whichis a major source of human mercury exposure, is found naturallyin fish, and is relatively stable. Ethyl mercury behavesin a similar fashion to methyl mercury at the cellular level,but with an excretory half-life about one third as long.Methyl mercury vapour is absorbed with similar (80%)efficiency as metallic mercury vapour. Intestinal absorptionof methyl mercury from fish is also fairly efficient, asis absorption through the skin. On entry to the bloodstream,methyl mercury adheres to sulfhydryl groups, particularlyto those in cysteine. Methyl mercury is depositedthroughout the body, with equilibrium between blood andbody occurring approximately four days after exposure.Distribution to peripheral tissues seems to occur throughone or more transporters, especially the cysteine transporter,probably adherent to the sulfhydryl group in cysteine.Concentration of methyl mercury occurs in the brain,liver, kidneys, placenta, and fetus, especially in the fetalbrain, as well as in peripheral nerves and bone marrow.Deposited methyl mercury slowly undergoes

demethylationto inorganic mercury.The excretory half-life of methyl mercury in man is about70 days, with approximately 90% being excreted in stool.Some degree of enterohepatic circulation apparently occurs.Perhaps 20% of methyl mercury is excreted in breast milk,with the actual amount varying with severity of exposure.Hair mercury reflects blood methyl mercury at the time ofincorporation, but not elemental mercury, and hence isnot a good index of total body burden, given the short half-life of methyl mercury in blood.Dimethyl mercury is also efficiently absorbed throughthe skin, and there is a reported death of a scientist causedby minimal skin contact[13].

Toxicity

Inorganic Mercury

Metallic Mercury Vapour:

Mercury in all forms poisonscellular function by altering the tertiary and quaternarystructure of proteins and by binding with sulfhydryl andselenohydryl groups. Consequently, mercury can potentiallyimpair function of any organ, or any subcellular structure.The chief target organ ofmercury vapour is the brain, but peripheralnerve function, renal function, immune function,endocrine andmuscle function, and several types of dermatitishave been described.With massive acute exposure to mercury vapour, erosivebronchitis and bronchiolitis potentially leading to respiratoryfailure may be accompanied by CNS symptoms such astremor or erethism.

Chronic exposure to clinically significant doses of mercuryvapour usually produces neurological dysfunction. Atlow-level exposures, nonspecific symptoms like weakness,fatigue, anorexia, weight loss, and gastrointestinal disturbancehave been described. Higher exposure levels areassociated with mercurial tremor: fine muscle fasciculationspunctuated every few minutes by coarse shaking. Erethismmay also be observed: severe behaviour and personality changes,emotional excitability, loss of

memory, insomnia, depression,fatigue, and in severe cases delirium and hallucination. Gingivitis and copious salivation have beendescribed.These symptoms may regress with cessation of exposure,but in many cases do not. Persistent neurological symptomsare common.

Mercurous Mercury:

Calomel (Hg2Cl2) is still used insome regions of the world as a laxative. Although poorly absorbed,some is converted to mercuric mercury, which is absorbed,and induces toxicity as expected with mercuric mercury.

MercuricMercury:

Acute poisoning with mercuric salts(typically HgCl2) generally targets the gastrointestinal tractand the kidneys. Extensive precipitation of enterocyte proteinsoccurs, with abdominal pain, vomiting, and bloodydiarrhoea with potential necrosis of the gut mucosa. Thismay produce death either from peritonitis or from septic orhypovolemic shock. Surviving patients commonly developrenal tubular necrosis with anuria.Chronic poisoning with mercury salts is rare, usually alsoinvolving concomitant occupational exposure to mercuryvapour. Kidney toxicity involves either renal tubular necrosisor autoimmune glomerulonephritis, or both. Immunedysfunctions include hypersensitivity reactions to mercuryexposure, including asthma and dermatitis, various typesof autoimmunity, and suppression of natural killercells and disruption of various other lymphocyte subpopulations.Brain dysfunction is less evident than with other formsof mercury. Thyroid dysfunction seems associated with inhibitionof the 5_ deiodonases, with decreased free T3 and increasedreverse T3. Accumulation in the testicles appearsto inhibit spermatogenesis. Atrophy and capillary damagehave been described in thigh muscle.

OrganicMercury:

Methylmercury reacts with sulfhydrylgroups throughout the body, therefore potentially interferingwith the function of any cellular or subcellular structure. Mercury is believed to interfere with DNA transcription andprotein synthesis, including protein synthesis in thedeveloping brain, with destruction of endoplasmic reticulumand disappearance of ribosomes. Evidence suggests disruptionof numerous subcellular elements in the central nervoussystem and other organs and in mitochondria; adverseeffects have also been described on heme synthesis,cell membrane integrity in many locations, free radicalgeneration, neurotransmitter disruption, andstimulation of neural excitoxins, resulting in damage tomany parts of the brain and peripheral nervous system.Methyl mercury has been associated with reduction inNatural Killer cell activity, as well as an imbalance Th2: Th1 ratios favouring autoimmunity.

Mercury is also possibly associated with disruption of DNArepair. The affinity of mercury for sulfhydryl groupsof the mitochondrial oxidative phosphorylation complexassociated with destruction of mitochondrial membranesmay contribute to chronic fatigue syndrome.

5. Clinical Presentation

Inorganic

Elemental (Metallic) Mercury:

Acute exposure to alarge quantity ofmercury vapour induces pneumonitis, as discussedpreviously. Symptoms of low-grade chronic exposureare more subtle and nonspecific: weakness, fatigue, anorexia,weight loss, and gastrointestinal distress, sometimes referredto as micromercurialism. At higher exposures, themercurial fine

tremor punctuated by coarse shaking occurs;erethism, gingivitis, and excessive salivation have also beendescribed, as has immune dysfunction.Objective findings include altered evoked potentialsand decreased peripheral nerve conduction velocity.Objective measures of short-term memory may be inverselycorrelated with urinary mercury in chloralkali workers.Reduced colour vision and visual acuity have also been observed. Changes in coordination, tremor, mental concentrationcapacity, facial expression, and emotional stateare also described, as are polyarthritis, various forms ofdermatitis, and a syndrome mimicking pheochromocytoma.Subtler clinical findings among dentists have been documented,including delayed reaction time, poor fine motorcontrol, and deficits in mental concentration, vocabulary,task switching, and the One Hole test, as well as mood lability,all correlating with urinary mercury excretion. Evidencealso links elemental mercury to depression, excessiveanger, and anxiety, as well as acute myocardial infarction,lipid peroxidation, and carotid atherosclerosis, in Finland; the Finnish experience may possibly be explainedby dietary selenium deficiency, since selenium antagonizesmercury toxicity. Other investigators, however, havedescribed associations between mercury and hypertension,lipid peroxidation, ischemic heart disease, and stroke[13].

Mercuric Salts:

Ingestion of mercuric chloride producesextensive precipitation of intestinal mucosal proteins,mucosal necrosis, generalized abdominal pain, bloody diarrhea,and shock. If the patient survives, acute renal failuremay follow.

Organic Mercury:

Methyl mercury and ethyl mercuryproduce similar signs and symptoms. Most published datarefer to methyl mercury. Symptoms relate more to magnitudeof methyl mercury retention than to the rate of deposition.Acute exposures tend to have a latency period of one ormore weeks; once acquired, toxic doses are cleared slowly, ifat all.Massive prenatal poisoning may induce a form of cerebralpalsy. Lesser prenatal doses have been associated withneuro-developmental delays and cognitive deficits.Postnatal exposures generate a range of symptoms rangingfrom paresthesias, with lesser exposures, to ataxia, visual,auditory, and extrapyramidal impairments with moderateexposures and clonic seizures in more severe exposures. Objective physical findings are similar to those seen withelemental mercury exposure.

Aim and Objectives

AIM AND OBJECTIVES:

AIM:

To purify calomel(பூரம்) and prepare Poora Parpam using traditional siddha methods with detailed study on acute and long term toxicity of “POORA PARPAM” in animal model (Wister albino rats)

OBJECTIVE:

1. Purification of POORAM using siddha literature
2. Preparation of POORA PARPAM using siddha literature
3. Chemical analysis of POORA PARPAM
4. Toxicity study on “POORA PARPAM” using animal models
    a. Acute toxicity
    b. Chronic toxicity

Materials and Methods

MATERIALS AND METHODS:

MATERIALS REQUIRED:

PURIFICATION:

1. Calomel (சுத்திசெய்யாதபூரம்)
2. Piper betel (கம்மாறுவெற்றிலை)
3. Piper nigrum(நல்லமிளகு)
4. துலாஎந்திரக்கருவி

DRUG PREPARATION:

1. Calomel(சுத்திசெய்தபூரம்)
2. Piper betel(கம்மாறுவெற்றிலை)
3. Boiled rice(வேகவைத்தஅரிசி)
4. Curcuma aromatic(மஞ்சள்)
5. Crab fat(நண்டு கொழுப்பு)

TOXICOLOGICAL STUDY:

Animals - Wistar albino rats (200 ± 25 g) bred in the animal house of GSMC, palayamkottai, were used. The animals were housed in wire-bottomed cages under a uniform condition of temperature and humidity and fed with normal food and tap water.

Chemical analysis:

1. Ammonium oxalate
2. Barium chloride
3. Silver nitrate
4. Con. Hydro chloric acid
5. Iodine solution

6. Glacial acetic acid
7. Potassium ferro cyanide
8. Con. Nitric acid
9. Ammonium thiocyanate
10. Ammonium molybdate
11. Esbatch's reagent
12. Ferric chloride
13. Potassium permanganate
14. Ninhydrin
15. Potassium ferrocyanide

METHODS:

PURIFICATION:

8.75g of leaves of piper betel leaves and 8.75g of black pepper are taken and grinded using water and is made in to a paste. This is then dissolved in 1.3L of water. This solution is kept in the lower vessel of Thulaaenthiram (துலாஎந்திரக்கருவி).

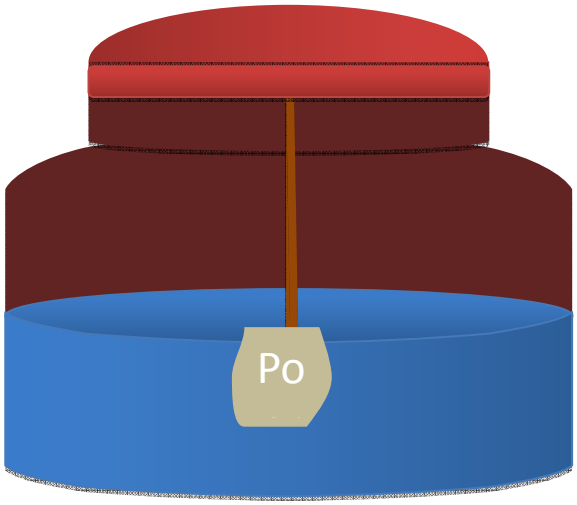


Figure 1: துலாஎந்திரக்கருவி

A single piece of pooram weighing around 35g is then tied in a thread and is allowed to hang inside the vessel containing solution. The whole setup is the heated from below till the amount of solution is reduced to 1/4th of the total amount. Then the pooram is washed and stored in a container.

DRUG PREPARATION:

A single piece of purified pooram is taken and is completely covered with the mixture of boiled rice and turmeric. This is then kept in a clay vessel and is heated from below.

Figure 2: Drug Preparation 1

Heat should be applied till the outer covering gets blackish colour. Same procedure is repeated 10 times.Then the processed piece of pooram is heated in a clay pot and crab fat is applied on the pooram piece, so that the piece absorbs the poured crab fat.This process should be done continuously for 24 hours. This is then cooled, made in to fine powder and is stored.

Figure 3: Poora Parpam Preparation

TOXICOLOGY STUDY:

SELECTION OF ANIMAL SPECIES:

Usually animal experiments are conducted on mice,albino rats,rabbit and dog.Young and immature animals should be selected for the study. In case of albino rats,it should be 180-200gm weight and 12 weeks growth.

PREPARATION OF ANIMALS:

Animals should be properly caged and should be fed properly with adequate diet. Allowthe animals to be in the cage for 5 days before drug administration,in order to make them accustomed to the new environment.The temperature maintained in the animal house should be 12 hours dark and the remaining 12 hours full of light.Only healthy animals should be selected for the study.

PREPARATION OF THE DRUG:

The drug used for animal study should be free from microbes.Highly irritant and highly toxic drugs should not be given to the animals.The drug must dissolve in any one of the suspending agents such as water,milk,honey, castor oil etc.

PREPARATION OF DOSES:

1. While doing animal study the dose of the drug given is determined on the basis of body weight of the animal.
2. In case of mice and albino rats, the dose of the drug must be 1 ml/ 100gm. body weight.
3. When water soluble drugs are given, it must be 2 ml/100 gm. body weight.
4. The adjuvant (அனுபானம்) used should be free from toxic properties.

ADMINISTRATION OF DRUG:

During drug administration care should be taken that the drug does not enter into the respiratory passage. Before drug administration,the animal has to be fasted.In case of albino rats the fasting period is 12hours.The weight of the animal has to be noted before drug administration. Then the drug is administered to the animal. Later the albino rats are fed with proper diet 1-2 hours and 3-4hours respectively after drug administration.

NUMBER OF ANIMALS AND DOSE LEVELS:

The dose of the drug given to the animal depends upon.

1. Body weight of the animal
2. Metabolic rate of the animal

While conducting acute toxicity study the number of animals in each group should be 5+5.Animals of both sex should be used.In case of chronic toxicity study the animals are divided into 4 groups,each group consisting of 20+20 animals.

OBSERVATION:

In acute toxicity study,the animals are carefully observed during the first 30 minutes and then observed for 24 hours.During that period,the animal may show changes in the skin, eye,mucous membrane,blood circulation,respiratory movements and the neurological problems may arise.

In case of sub-acute toxicity study the animals have to be observed for 90 days or sometimes up to 1 year .Some researchers conduct the chronic toxicity study for the whole lifetime of the animal.

BODY WEIGHT OF THE ANIMAL:

The weight of the animal must be taken four times during the course of study.

i. First before drug administration.
ii. One Week after drug administration.
iii. Two weeks after drug administration.
iv. Before sacrificing the animal.

DATA AND REPORT:

At the end of the animal study,the following data must be given.

1.Number of animals selected for the study.

2.Number of animals died due to the toxicity of the drug given.

3.Number of animals sacrificed at the end of animal study.

4.Changes in animal behaviour due to acute and chronic toxicity.

5.Histo-pathological changes in the internal organs such as liver, kidney and heart.

CHRONIC TOXICITY STUDY

1. This experiment has to be carried out 90 days to one year or one year to five years or entire life span of the animal.
2. Observe the animal daily and record the findings observe for cumulative effect of toxicity.

CHEMICAL ANALYSIS:

PREPARATION OF EXTRACT:

100mgs of the drug is weighed accurately and placed in a clean beaker and few drops of Con. Hcl is added and allowed to evapourate. Then it is allowed to cool and few drops of Con. Nitric acid is added. It is then allowed to cool and 20ml of distilled water is added so that it gets dissolved in it. This is then transferred to 100ml volumetric flask and is made up to 100ml with distilled water. This is then mixed, filtered and is taken for analysis.

TEST FOR CALCIUM:

2ml of the extract is taken in a clean test tube and 2ml of 4% ammonium oxalate solution is added to it. Appearance of white precipitate indicates the presence of calcium.

TEST FOR SULPHATE:

2ml of the extract is added to 5% barium chloride solution. Appearance of white precipitate indicates the presence of sulphate.

TEST FOR CHLORIDE:

Extract is treated with silver nitrate solution. Appearance of white precipitate indicates the presence of chloride.

TEST FOR CARBONATE:

The substance is treated with concentrated hydrochloric acid. Appearance of brisk effervescence indicates the presence of sulphate.

TEST FOR STARCH:

The extract is added with weak iodine solution. Formation of blue colour indicates the presence of starch.

TEST FOR IRON:

The extract is acidified with glacial acetic acid and potassium ferrocyanate is added. Formation of blood red colour indicates the presence of ferrous iron.

TEST FOR PHOSPHATE:

The extract is treated with ammonium molybdate and concentrated nitric acid. Appearance of yellow precipitate indicates the presence of phosphate.

TEST FOR ALBUMIN:

Extract is treated with Esbatch's reagent. Formation yellow precipitate indicates the presence of albumin.

TEST FOR TANNIC ACID:

The extract is treated with ferric chloride. Appearance of black precipitate indicates the presence of tannic acid.

TEST FOR UNSATURATION:

Potassium permanganate is added to the extract. Decolourisation of the solution indicates the presence of unsaturated fatty acids

TEST FOR REDUCING SUGAR:

5ml of benedict's solution is taken in a test tube and allowed to boil for 2 minutes. Then 8-10 drops of extract is added to it and is boiled for 2 minutes. Significant colour change indicates the presence of reducing sugar.

TEST FOR AMINO ACID:

One or two drops of the extract is placed on a filter paper and dried. After drying 1% Ninhydrin is sprayed over it and dried. Formation of violet colour indicates the presence of amino acid.

TEST FOR ZINC:

The extract is treated with potassium ferro cyanide. Appearance of white precipitate indicates the presence of zinc.

RESULTS

RESULTS:

PURIFICATION:

Weight of raw pooram – 200g

Weight of piper betel – 54g

Weight of piper nigrum – 54g

Amount of water – 6L

Weight of pooram after purification – 192g

The above data's showed that their is loss of total of 8g from 200g of pooram taken for purification. Totally there is loss of 4% of raw drug after purification.

POORA PARPAM – PREPARATION:

Weigth of purified Pooram – 192g

Amount of boiled rice – 250g

Amount of turmeric powder – 100g

Total No. of Crabs – 200 (6.5 kgs)

Weight of Poora parpam before grinding – 190g

Weight of Poora parpam after grinding – 185g

The above data's indicate that 185g of pooraparpam is prepared from 192g of purified pooram with 3.2% weight loss.

CHEMICAL ANALYSIS:

Table 3: Chemical Analysis of Poora Parpam

S.No	Substance	Result
1	Calcium	+
2	Sulphate	+
3	Chloride	+
4	Carbonate	-
5	Starch	-
6	Ferric iron	-
7	Ferrous iron	+
8	Phosphate	-
9	Albumin	-
10	Tannic acid	-
11	Unsaturated compounds	+
12	Reducing sugar	-
13	Amino acid	-
14	Zinc	-

Data's in the above table indicates that small amount of unsaturated compounds, ferrous iron, chloride, sulphate and calcium are present in Poora Parpam.

TEST FOR METALS:

Table 4: Test for Metals in Poora Parpam

S.No	Metals	Amount
1	As193.696 (Arsenic)	BDL
2	Cd 226.502 (Cadmium)	BDL
3	Cu 324.754 (Copper)	BDL
4	Hg253.652 (Mercury)	3.421mg/L
5	Pb 230.204 (Lead)	BDL

BDL = Below detection limit

The above data show that mercury is present in large quantity in the drug. But all other metals such as lead, cadmium, copper, and arsenic are below detection limits.

Total amount of poora parpam in 1000ml of sample = 1000mg

That implies 1000mg of Poora Parpam has 3.421mg of mercury

FOURIER TRANSFORMINFRARED SPECTROMETRY REPORT:

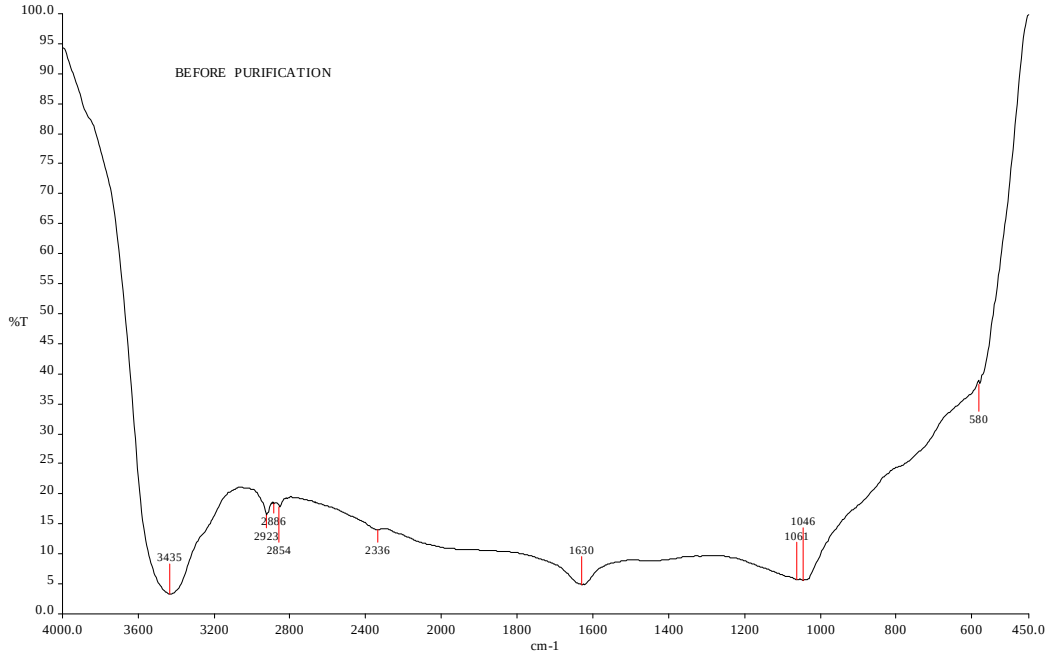


Figure 4: FTISR Raw Pooram

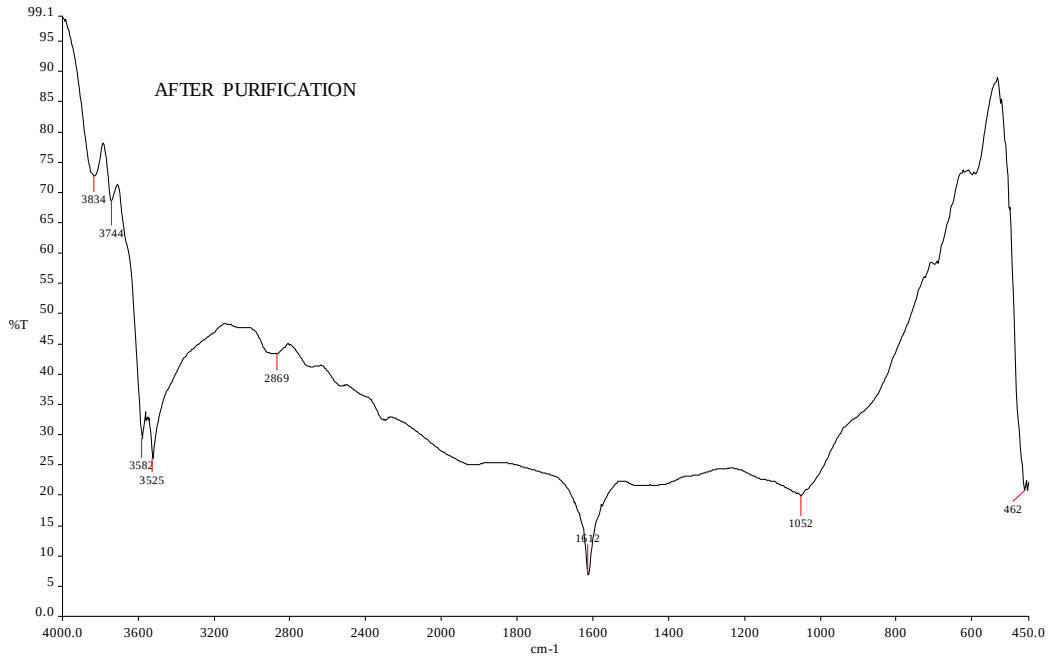


Figure 5: FTISR Purified Pooram

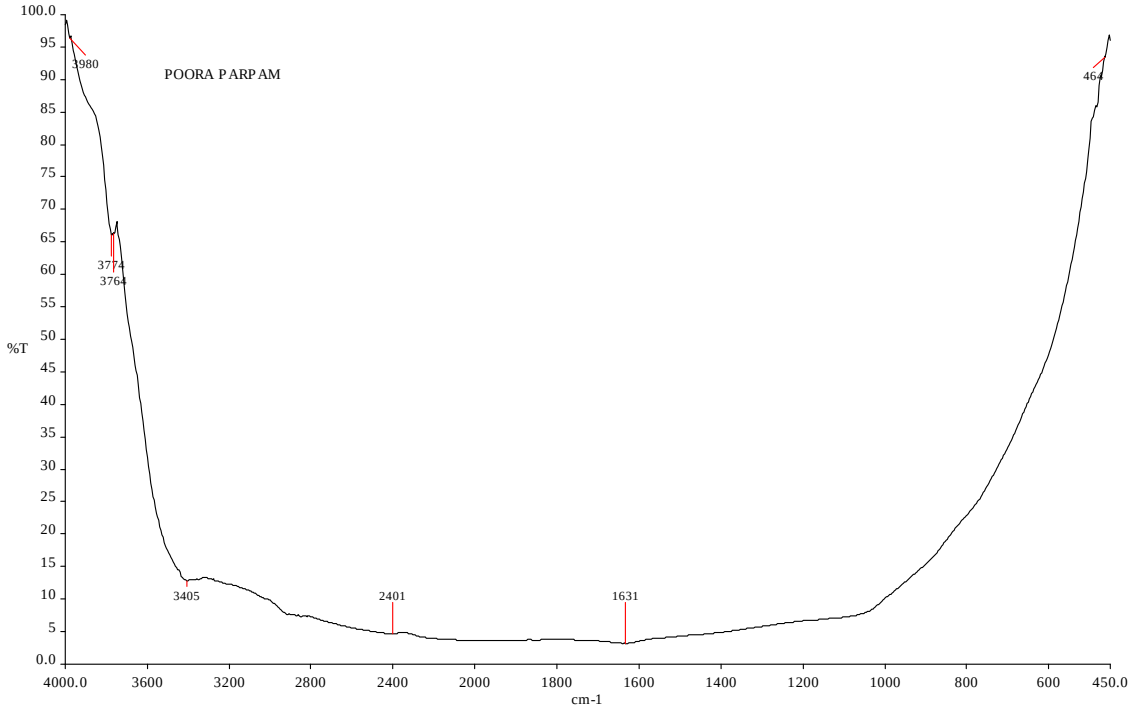


Figure 6: FTISR Poora Parpam

TOXICITY STUDY:

The toxicity evaluation of PooraParpam is carried in two phases.

Phase I	-	Acute toxicity study.
Phase II	-	Chronic toxicity study.

ACUTE TOXICITY STUDY

Animals

Wister albino rats bred in the animal house attached to the pharmacology Department, Government Siddha Medical College, Palayamkottai were used.

Sex

Animals of both sexes were used.

Weight

Animals weighing between 80-120 gm. were selected.

Food and water

The animals were maintained with standard animal feed and water ad-libitum.

Number of Animals

24 Albino rats divided into 6 groups each group consisting of 4 rats.

Dose Levels

The following dose levels were fixed by presuming range of least toxic to high toxic doses.

I Group	-	Control
II Group	-	40 mg/100 gm body weight of the animal.
III Group	-	80 mg/100 gm body weight of the animal.
IV Group	-	160 mg/100 gm body weight of the animal.
V Group	-	320 mg/100 gm body weight of the animal.
VI Group	-	640 mg/100 gm body weight of the animal.

Route of administration

The drug was administered orally.

Drug preparation

The drug was weighted and taken and suspended in castor oil. The mixture was ground well before the administration. The preparation was done in such a way that 1ml of suspension contains dose ranging from 40mg to 640 mg of Poora Parpam which is given to the respective groups, as classified above in the doses level. The drug was administrated in morning and observed.

Observation

The following details were recorded

CENTRAL EFFECTS:

I. Stimulation

1. Hyperactivity
2. Pyloerection
3. Twitching
4. Rigidity
5. Irritability
6. Jumping
7. Clonic convulsions
8. Tonic convulsions

II. Depression

1. Ptosis
2. Sedation
3. Sleep
4. Loss of traction

5. Loss of pinna reflex
6. Ataxia
7. Loss of muscle tone
8. Analgesia

III. Autonomic Effects

1. Straub tail
2. Laboured respiration
3. Cyanosis
4. Blanching
5. Reddening
6. Abnormal secretions

At the end of 24 hours the number of animals live or dead in each group was noted and the approximate LD 50 was determined. The animals were morphologically examined for any toxic symptoms.

CHRONIC TOXICITY STUDY:

Animals

Wister albino rats bred in the animal house attached to the Pharmacology Department, Government Siddha Medical College, Palayamkottai were used.

Sex

Animals of both sexes were used.

Weight

Animals weighing between 80-120 gm. are selected.

Food and water

The animals were maintained with standard animal feed and water ad-libitum.

Number of Animals

12 Albino rats are divided into 3 groups each group consisting of 4 rats.

Dose Levels

Two doses were selected from the acute toxicity study. These doses did not have any acute toxicity effect and presumed to be safe for long term administration in animals.

I Group	-	Control
II Group	-	40mg / 100 gm. body weight of the animal.
III Group	-	80mg / 100 gm body weight of the animal.

Route of administration

The drug was administered orally for about 3 months.

Drug preparation

The drug was weighted and taken and suspended in Ghee, the mixture was ground well before the administration. The preparation was done in such a way that 1 ml of suspension contains dose ranging from 40 mg/ml and 80mg/ml of Poora Parpam for the groups taken. The prepared drug was administrated once a day (morning) for 90 days.

Observation

The following details were recorded before and after the drug administration.

Body weight of the animal

Haematological investigation

1. W.B.C Total count
2. W.B.C Differential count
3. Haemoglobin

Every month and at the end of the experiment, the above parameters were recorded and the resultsare tabulated.

One animal from each group, were sacrificed at the end of the experiment and were dissected. The visceral organs like Liver, Kidney and Heart were removed from each animal and were preserved in 40% formalin solution send for Histo-pathological studies.

Histo-pathological procedure:

The sections were stained with haemotoxillin and eosin and the histo-pathological report was given by Dr.Swaminathan, Professor Pathology Department, Tirunelveli Medical College.

The tabular column shown in tested parameters and changes in histo-pathological specimens were also documented.

Table 5: Acute Toxicity Study of Poora Parpam at control

Observation	At 1 hr	At 2 hrs	At 4 hrs	At 24 hrs
I.Stimulation:				
Hyperactivity	-	-	-	-
Pyloerection	-	-	-	-
Twitching	-	-	-	-
Rigidity	-	-	-	-
Irritability	-	-	-	-
Jumping	-	-	-	-
Clonic convulsions	-	-	-	-
Tonic convulsions	-	-	-	-
II.Depression:				
Ptosis	-	-	-	-
Sedation	-	-	-	-
Sleep	-	-	-	-
Loss of traction	-	-	-	-
Loss of pinna reflex	-	-	-	-
Ataxia	-	-	-	-
Loss of muscle tone	-	-	-	-
Analgesia	-	-	-	-
III. Autonomic effect:				
Straub tail	-	-	-	-
Laboured respiration	-	-	-	-
Cyanosis	-	-	-	-
Blanching	-	-	-	-
Reddening	-	-	-	-
Abnormal Secretions	-	-	-	-
IV.Number of dead after 24 hrs:	-	-	-	-

--Negative + Positive

Table 6: Acute toxicity study at a dose of 40mg/100 gm body weight

Observation	At 1 hr	At 2 hrs	At 4 hrs	At 24 hrs
I.Stimulation:				
Hyperactivity	-	-	-	-
Pyloerection	-	-	-	-
Twitching	-	-	-	-
Rigidity	-	-	-	-
Irritability	-	-	-	-
Jumping	-	-	-	-
Clonic convulsions	-	-	-	-
Tonic convulsions	-	-	-	-
II.Depression:				
Ptosis	-	-	-	-
Sedation	-	-	-	-
Sleep	-	-	-	-
Loss of traction	-	-	-	-
Loss of pinna reflex	-	-	-	-
Ataxia	-	-	-	-
Loss of muscle tone	-	-	-	-
Analgesia	-	-	-	-
III. Autonomic effect:				
Straub tail	-	-	-	-
Laboured respiration	-	-	-	-
Cyanosis	-	-	-	-
Blanching	-	-	-	-
Reddening	-	-	-	-
Abnormal Secretions	-	-	-	-
IV.Number of dead after 24 hrs:	-	-	-	-

--Negative + Positive

Table 7: Acute Toxicity Study at a dose of 80mg/100 gm body weight

Observation	At 1 hr	At 2 hrs	At 4 hrs	At 24 hrs
I.Stimulation:				
Hyperactivity	-	-	-	-
Pyloerection	-	-	-	-
Twitching	-	-	-	-
Rigidity	-	-	-	-
Irritability	-	-	-	-
Jumping	-	-	-	-
Clonic convulsions	-	-	-	-
Tonic convulsions	-	-	-	-
II.Depression:				
Ptosis	-	-	-	-
Sedation	-	-	-	-
Sleep	-	-	-	-
Loss of traction	-	-	-	-
Loss of pinna reflex	-	-	-	-
Ataxia	-	-	-	-
Loss of muscle tone	-	-	-	-
Analgesia	-	-	-	-
III. Autonomic effect:				
Straub tail	-	-	-	-
Laboured respiration	-	-	-	-
Cyanosis	-	-	-	-
Blanching	-	-	-	-
Reddening	-	-	-	-
Abnormal Secretions	-	-	-	-
IV.Number of dead after 24 hrs:	-	-	-	-

--Negative + Positive

Table 8: Acute Toxicity Study at a dose of 160mg/100 gm body weight

Observation	At 1 hr	At 2 hrs	At 4 hrs	At 24 hrs
I.Stimulation:				
Hyperactivity	-	-	-	-
Pyloerection	-	-	-	-
Twitching	-	-	-	-
Rigidity	-	-	-	-
Irritability	-	-	-	-
Jumping	-	-	-	-
Clonic convulsions	-	-	-	-
Tonic convulsions	-	-	-	-
II.Depression:				
Ptosis	-	-	-	-
Sedation	-	-	-	-
Sleep	-	-	-	-
Loss of traction	-	-	-	-
Loss of pinna reflex	-	-	-	-
Ataxia	-	-	-	-
Loss of muscle tone	-	-	-	-
Analgesia	-	-	-	-
III. Autonomic effect:				
Straub tail	-	-	-	-
Laboured respiration	-	-	-	-
Cyanosis	-	-	-	-
Blanching	-	-	-	-
Reddening	-	-	-	-
Abnormal Secretions	-	-	-	-
IV.Number of dead after 24 hrs:	-	-	-	-

--Negative + Positive

Table 9: Acute Toxicity Study at a dose of 320mg/100 gm body weight

Observation	At 1 hr	At 2 hrs	At 4 hrs	At 24 hrs
I.Stimulation:				
Hyperactivity	-	-	-	-
Pyloerection	-	-	-	-
Twitching	-	-	-	-
Rigidity	-	-	-	-
Irritability	-	-	-	-
Jumping	-	-	-	-
Clonic convulsions	-	-	-	-
Tonic convulsions	-	-	-	-
II.Depression:				
Ptosis	-	-	-	-
Sedation	-	-	-	-
Sleep	-	-	-	-
Loss of traction	-	-	-	-
Loss of pinna reflex	-	-	-	-
Ataxia	-	-	-	-
Loss of muscle tone	-	-	-	-
Analgesia	-	-	-	-
III. Autonomic effect:				
Straub tail	-	-	-	-
Laboured respiration	-	-	-	-
Cyanosis	-	-	-	-
Blanching	-	-	-	-
Reddening	-	-	-	-
Abnormal Secretions	-	-	-	-
IV.Number of dead after 24 hrs:	-	-	-	-

--Negative + Positive

Table 10: Acute Toxicity Study at a dose of 640mg/100 gm body weight

Observation	At 1 hr	At 2 hrs	At 4 hrs	At 24 hrs
I.Stimulation:				
Hyperactivity	-	-	-	-
Pyloerection	-	-	-	-
Twitching	-	-	-	-
Rigidity	-	-	-	-
Irritability	-	-	-	-
Jumping	-	-	-	-
Clonic convulsions	-	-	-	-
Tonic convulsions	-	-	-	-
II.Depression:				
Ptosis	-	-	-	-
Sedation	-	-	-	-
Sleep	-	-	-	-
Loss of traction	-	-	-	-
Loss of pinna reflex	-	-	-	-
Ataxia	-	-	-	-
Loss of muscle tone	-	-	-	-
Analgesia	-	-	-	-
III. Autonomic effect:				
Straub tail	-	-	-	-
Laboured respiration	-	-	-	-
Cyanosis	-	-	-	-
Blanching	-	-	-	-
Reddening	-	-	-	-
Abnormal Secretions	-	-	-	-
IV.Number of dead after 24 hrs:	-	-	-	-

--Negative + Positive

Acute Toxicity Study

The said parameters in acute toxicity study were observed on six groups (Group I, II, III, IV, V, VI). Group II, III, IV, V, VI were administrated with drugs such as 40mg, 80mg, 160mg, 320mg, 640mg /100 gm body weight of the animal respectively.

The results were tabulated in the table 1 to 6. From the table 2 to 6 it being found that the drug Poora Parpam did not produce any mortality even upto 320mg /100 gm body weight of the animal.

S.No	Blood	At O' day (Mean)	At 30th day (Mean)	At 90th day (Mean)
1	WBC Total count	8900/cumm	9100/cumm	9200/cumm
2	Differential Count			
	Neutrophil	28%	26%	24%
	Eosionophil	-	-	-
	Basophil	-	-	-
	Lymphocyte	72%	74%	76%
	Monocyte	-	-	-
3.	Haemoglobin %	66	68	70
4.	Body Weight	100 gm	102 gm	104 gm

TABLE NO:8

Changes in the parameters of weight and Hematological indices

Group II animals: 40mg / 100mg body weight of the animal

S.No	Blood	At O' day (Mean)	At 30th day (Mean)	At 90th day (Mean)
1	WBC Total count	9500/cumm	9700/cumm	9800/cumm
2	Differential Count			
	Neutrophil	32%	28%	24%
	Eosionophil	-	-	-
	Basophil	-	-	-
	Lymphocyte	68%	72%	76%
	Monocyte	-	-	-
3.	Haemoglobin %	68	70	72
4.	Body Weight	100 gm	105 gm	110 gm

TABLE NO:9

Changes in the parameters of weight and Hematological indices

Group III animals: 80mg / 100mg body weight of the animal

S.No	Blood	At O' day (Mean)	At 30th day (Mean)	At 90th day (Mean)
1	WBC Total count	9200/cumm	9400/cumm	9600/cumm
2	Differential Count			
	Neutrophil	30%	26%	20%
	Eosionophil	-	2	2
	Basophil	-	-	-
	Lymphocyte	70%	72%	78%
	Monocyte	-	-	-
3.	Haemoglobin %	66	68	70
4.	Body Weight	100 gm	110 gm	120 gm

Table 10

Acute Toxicity Study Analysis

Group	Dose in mg/100gm body weight of animal	No of rats	No of rats died
II	40	4	-
III	80	4	-
IV	160	4	-
V	320	4	-
VI	640	4	-

Since there is no mortality of the animal in Acute toxicity study, lethal dose of drug need not be calculated.

Table 11

Chronic Toxicity Study Analysis

Group	Dose in mg/100gm body weight of animal	No of rats	Days	No of rats died
I	40	4	0	-
			30	-
			90	-
II	80	4	0	-
			30	-
			90	-

Median Lethal Dose (LD 50):

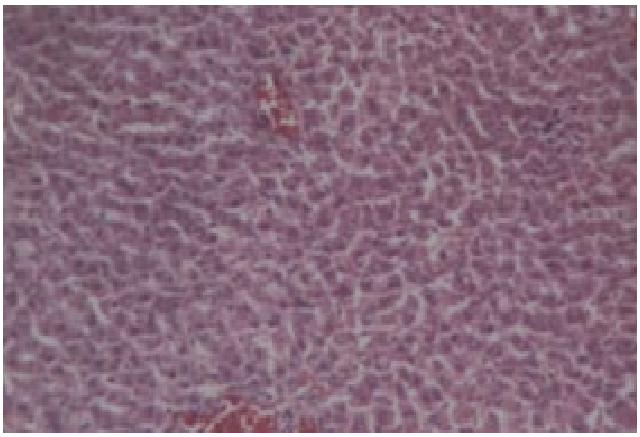
It is the dose which kills half the population of the animal tested.

Since there is no mortality of the animal in chronic toxicity study, lethal dose of drug need not be calculated.

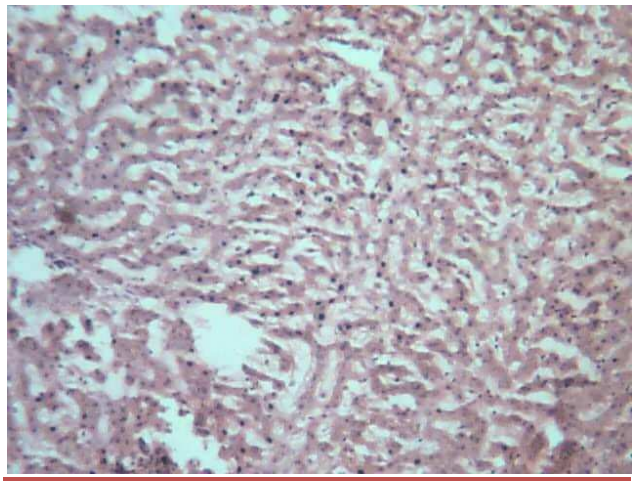
In case of Chronic Toxicity Study, with the help of physiological parameter such as haematological & Histopathological studies the drug reaction within the animal can be assessed and being tabulated respectively.

HISTO-PHATHOLOGY STUDY

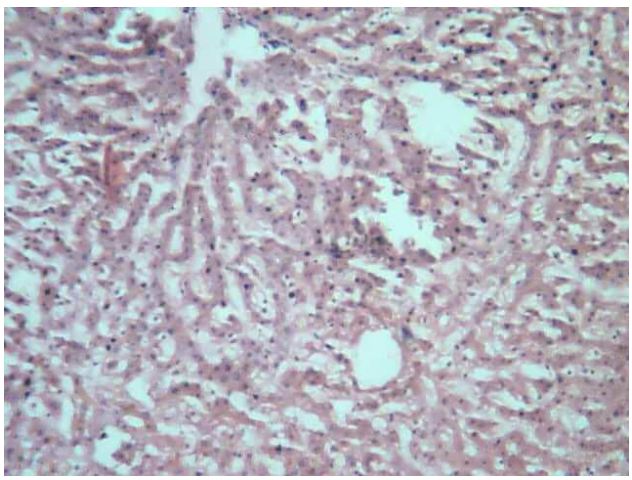
HISTOPATHOLOGY OF LIVER OF RAT:



Control: Section studied shows normal liver tissue

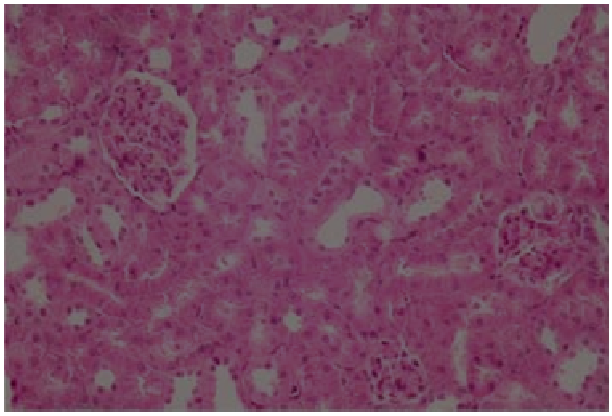


Low Dose Exposure: Section studied shows liver tissue with dilated central vein with congested sinusoids.

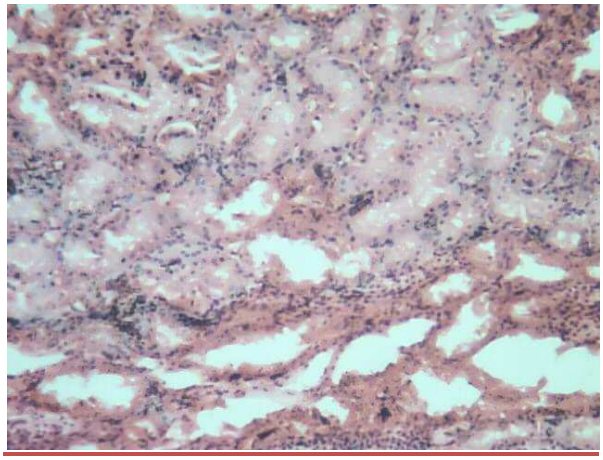


High Dose Exposure: Section studied shows liver tissue with dilated central vein with congested sinusoids.

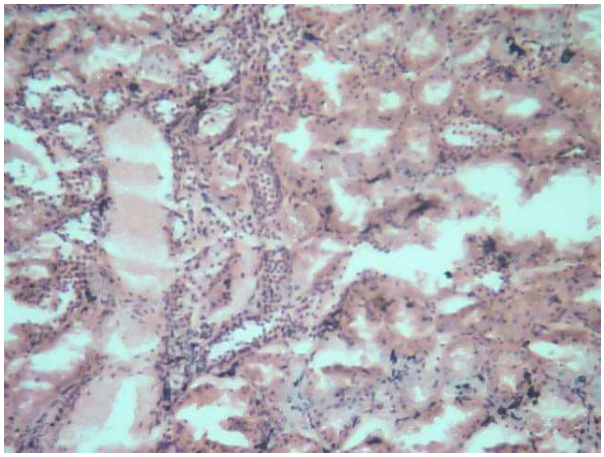
HISTO-PHATHOLOGY OF KIDNEY OF RAT:



Control: Section studied shows normal kidney tissue

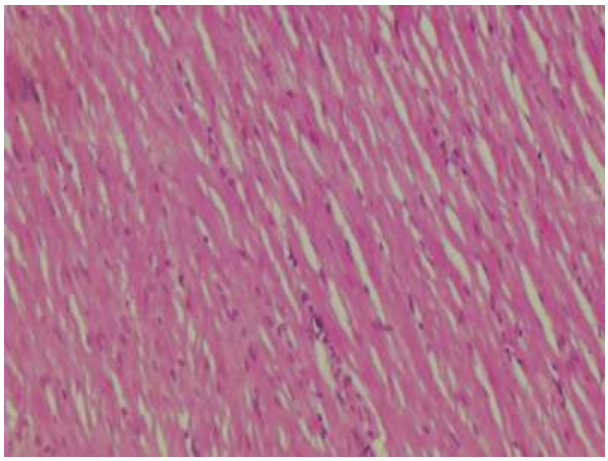


Low Dose Exposure: Section studied shows normal glomeruli with focal cloudy swelling of the tubules

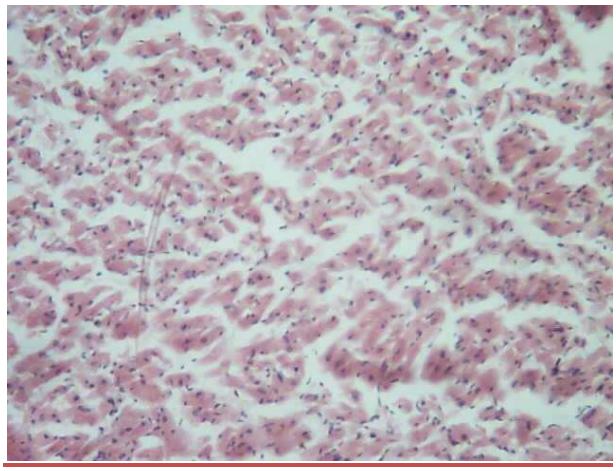


High Dose Exposure: Section studied shows normal glomeruli with focal cloudy swelling of the tubules

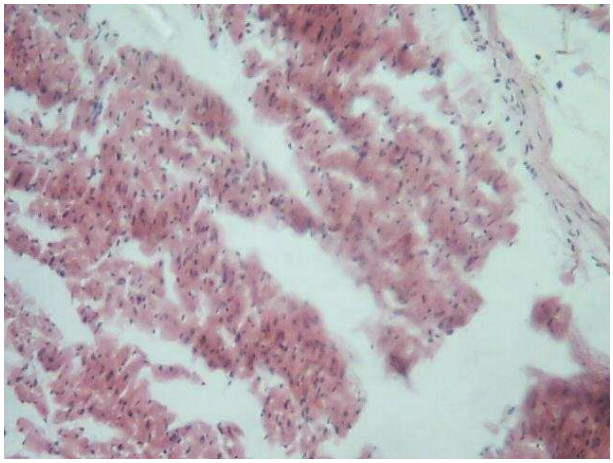
HISTO-PHATHOLOGY OF HEART OF RAT:



Control: Section studied shows normal heart tissue



Low Dose Exposure: Section studied shows normal bundles of myocardial fibers.



High Dose Exposure: Section studied shows normal bundles of myocardial fibers.

Discussion

DISCUSSION:

According to the research done so far, the amount of mercury in Poora Parpam is around 3.42µg/g. The therapeutic dose of Poora Parpam is usually 65mg/dose with consumption of three times a day. That shows if a person consumes Poora Parpam under these regulations, total intake in a week will be 1.2mg. Which implies total intake of mercury in a week will be 4.1µg. In 2004 the Joint FAO/WHO Expert Committee on Food Additives (JECFA) established a tolerable intake of 1.6 µg/kg bodyweight per week for methylmercury in order to protect the developing fetus from neurotoxic effects.For adults, up to about twice the tolerable intake per week would not pose any risk of neurotoxicity.So amount of mercury present in Poora Parpam is slightly (0.9µg)higher than permissible limits of mercury for a week in adults. But ingestion of 10times the dosage of drug doesn't showed any notable toxic symptoms in animals. This contrary result in animal study may be due to the fact that the drug is administered along with castor oil as adjuvant, which may play an important role in reducing its toxic properties. Moreover, the permissible limits regulations by WHO applies mainly to long term exposure to mercury for months. But usually the drug is given only for a week.

In case of humans, some factors such as food habits may also play an important role in determining the toxicity of mercury-containing drugs. Because most of the toxicity work done by WHO is on western population, which follows very different food habits compared with a normal Indian population. For example, intake of common food ingredients such as sesame oil, turmeric, tamarind, garlic, and asafoetida may play an important role in prevention of toxic effects of mercury. This becomes more evident from the south Indian population which consumes sea food in large amount. A recent research suggest that average mercury concentration obtained in muscle of deep sea fishes that is regularly consumed by south-east Indian

population was 1.6 mg/kg dry weight (0.352 mg/kg wet weight), which is higher than the prescribed limits (0.3 mg/kg wet weight). But there are no notable toxic effects due to mercury such as Alzeimer's disease, autism in south indian population when compared with the western population. This may be due to the protective mechanism of indian food ingredients.

In histo-pathology studies, traces of mercury are present in liver and kidney. But this may be reversible, as it didn't produce any significant toxic symptom in animals. Usually metallothionins – a cysteine rich protein plays an important role in protection against mercury toxicity in tissues by binding with mercury. But excretion of mercury from kidney may take a long time as mercury gets deposited in glomerular tissues due to effective tubular reabsorption. However, presence of metallothionins protects liver and kidney from effective damage though it won't play any effective role in removal of mercury from our body. Various cell culture studies have shown that turmeric, garlic and tamarind plays an important role in increasing metallothionin production in cultured cells. These data's further supports the proposed mechanism of protective role of food diets in Indian population against mercury.

Another unexplored facet, which could affect the efficacy and toxicity of these drugs, are drug-drug interaction that occurs when they are given in combination with other herbal preparations. The fact that mercury sulfide is insoluble and does not get absorbed through blood circulation eliminates its chances of providing therapeutic benefits, since it may not react at all with the cell receptors. However, incorporation of herbal ingredients in these preparations may alter the cell uptake, distribution, and elimination profile as well as the therapeutic properties. So a detailed study on all these factors is necessary.

Summary:

This study aims at evaluating the toxicity profile of Poora Parpam, commonly used siddha drug in treatment of various metabolic disorders. Raw Pooram is first purified using piper betel and piper longum, and Poora parpam is then prepared using unique method mentioned in Aruvai maruthuvam. Basic chemical analysis was performed to study the presence of various elements present in the drug along with detailed toxicology study using animal models. According to the chemical analysis done, the amount of mercury in Poora Parpam is around 3.42µg/g. The therapeutic dose of Poora Parpam is usually 65mg/dose with consumption of three times a day. That shows if a person consumes Poora Parpam under these regulations, total intake in a week will be 1.2mg. Which implies total intake of mercury in a week will be 4.1µg. But this amount of mercury present in Poora Parpam is slightly (0.9µg) higher than permissible limits of mercury for a week in adults declared by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) In 2004.

In contrary to the chemical analysis, administration of 10 times the therapeutic dosage in acute toxicity study doesn't show any notable toxic symptoms in animals. This may be due to the fact that the drug is administered along with castor oil as adjuvant, which may play an important role in reducing its toxic properties. Moreover, the permissible limits regulations by WHO applies mainly to long term exposure to mercury for months. But usually the drug is given only for a week.

In chronic studies, Histo-pathology of kidney showed normal glomeruli with focal cloudy swelling of the tubules. But this may be reversible, as it didn't produce any significant toxic symptom in animals. Another unexplored facet, which could affect the efficacy and toxicity of these drugs, are drug-drug interaction that occurs when they are given in combination with other herbal preparations. . Although Poora

Parpam have metal contents far greater than the WHO limits, the toxicity of a preparation need not directly correlate with the metal content in the sample. The chemical nature of the metal, route of administration, dosage, residence time within the body, pharmacokinetics and dynamics, bioavailability, metabolic transformations of the preparation, age, gender, physiology, nature and stage of disease, and diet can influence the toxic manifestations of the drug. Hence a detailed study on all these factors is essential to answer the comprehensions raised by the usage of herbo-metallic drugs like Poora Parpam.

CONCLUSION

CONCLUSION:

Even though the metals are purified and believed to be non-toxicaccording to Siddha system, this only refers to the clinical ortherapeutic dose, which isminimal. So over consumption due to improper medication/self-medication may lead to significant toxic effects. Although most of the siddha medicinalpreparations have metal contents far greater than the WHOlimits, the toxicity of a preparation need not directly correlatewith the metal content in the sample. The chemical nature ofthe metal, route of administration, dosage, residence timewithin the body, pharmacokinetics and dynamics, bioavailability,metabolic transformations of the preparation, age,gender, physiology, nature and stage of disease, and diet caninfluence the toxic manifestations of the herbo-metallicpreparations. Therefore, a careful analysisof all these parameters is required in order to establish the riskinvolved in a given herbo-metallic preparation.Most of the studies conducted thus far on mercury-based siddha medicine preparations in experimental animals have been short-term toxicity studies with use of high doses of HgS, which cannot be correlated with humans. Variations in therapeutic doses are recommended by practitioners for different ailments. Practioners in siddha medicines adopt a holistic approach to treatment and consider the physiological aspects of an individual along with the type of disease and stage of presentation. Diet restrictions also contribute toalterations in the pharmacokinetics, and thus labeling a traditional medicine preparation as toxic based only on the metal content seems inappropriate. However, in-depth and systematic investigations are not available for these preparations.Pre-clinical studies are needed after conversion ofthe human therapeutic dose to an animal dose, and bothshort-term and long-term toxicity have to be evaluated.

Significant and substantial amount of data through thesestudies can provide a platform for designing human clinicaltrials. Even though cinnabar has beenused for centuries in traditional medicine, pharmaco-vigilancenever existed then and does not even prevail in the modern era. The need for patient follow-up after counselingand drug therapy was rare in earlier times, and even now it isnot followed stringently. Hence, scientific evidence is lackingto confirm the safety and efficacy of these drugs. No pharmco-therapeutic studies existto analyze the benefits of these drugs. Shortcomings inchoice of animal models and proper design of experiments toassess toxicity have hampered the risk assessment of thesetraditional preparations, and hence there is a requirement formore comprehensive studies to understand the ramificationsof these therapeutic processes.

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14. **வைத்திய இரத்தின சுருக்கம்** 360
15. **வைத்திய திறவுகோல்**
16. **அகத்தியர் பரிபூரனம்** 400
17. **சித்தமருத்துவ செய்பெரு முறைகள்**
18. **ஆத்மரட்சாமிர்த வைத்திய சாரசங்கிரகம்**
19. **சித்த வைத்திய திரட்டு**
20. **யாக்கோபு திருவாய் மலர்த்தருளிய பெருநூல் –சன்ன காண்டம்** 600
21. **சிகிச்சா ரத்ன தீபம்**